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=> d his
     (FILE 'USPAT' ENTERED AT 10:01:27 ON 19 MAR 1997)
L1          4827 S PAPILOMAVIRUS OR PV
L2           446 S HUMAN AND L1
L3             0 S L2 AND HPV18
L4            15 S "L1" AND "L2" (P) L2
L5          3705 S VACCINE
L6            42 S L5 AND L2
L7             1 S L6 AND HPV-18
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> d l5 all

L5 ANSWER 1 OF 1 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 93-320439 [40] WPIDS
DNC C93-142573
TI Treatment of AIDS-associated optic neuropathy - by oral admin. of pentoxifylline and other tumour necrosis factor blockers.
DC B02
IN DUGEL, P U; **GILL, P S**; MADIGAN, M; SADUN, A A
PA (UYSC-N) UNIV SOUTHERN CALIFORNIA
CYC 42
PI WO 9318770 A1 930930 (9340)* EN 25 pp A61K031-52
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US
AU 9348085 A 931021 (9407) A61K031-52
ADT WO 9318770 A1 WO 93-US2704 930324; AU 9348085 A AU 93-48085 930324
FDT AU 9348085 A Based on WO 9318770
PRAI US 92-858129 920326
REP 1.Jnl.Ref
IC ICM A61K031-52
AB WO 9318770 A UPAB: 931129
Treatment of a subject displaying optic neuropathy associated with AIDS comprises orally administering an amt. (pref. 200mg-1g per dose, 2-4 times per day) of pentoxifylline (I) effective to prevent or reduce the expression of tumour necrosis factor (TNF) or neutralise TNF in the CNS.

Also claimed are the prevention or redn. of the expression of TNF or neutralisation of TNF in the CNS in methods for treatment of optic neuropathy associated with AIDS and for treatment of CNS impairment as displayed with AIDS; and for treatment of a subject displaying at least one CNS impairment, such as an immune disorder disease.

More specifically, the immune disorder diseases include multiple sclerosis, optic neuritis, Devic's disease or demyelinating processes.

USE - The effective use of (I) (a TNF blocker) is based on the hypothesis that TNF may be involved in mediating neural damage in the CNS and optic nerve, as in AIDS.

Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B04-A06; B04-B03A; B12-A06; B12-C10; B12-D02A; B12-L04

$$\int_0^{16^\circ} \not{\alpha}\, d\alpha$$

> d l11 1-15

L11 ANSWER 1 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-402302 [37] WPIDS
DNC C97-129737
TI Enhancing oral absorption of taxane - by co-administration of cinchonine, for treatment of tumours etc..
DC B02
IN HANSEL, S B
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 70
PI WO 9727855 A1 970807 (9737)* EN 12 pp A61K031-44
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
ADT WO 9727855 A1 WO 97-US405 970115
PRAI US 96-10916 960131
IC ICM A61K031-44
ICS A61K031-47

L11 ANSWER 2 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-204369 [19] WPIDS
DNC C97-065743
TI Purificn. of ethoxylated fat - by treatment with solid mixt. of aluminium oxide and silicate.
DC B05 B07
IN DRALLE-VOSS, G; LANG, S; SAUPE, T; STOSSER, M; ZIPPLIES, M; LAND, S; STOESSER, M; DRALLEVOSS, G
PA (BADI) BASF AG
CYC 41
PI DE 19536165 A1 970403 (9719)* 4 pp C07C067-56
WO 9712017 A1 970403 (9719) DE 14 pp C11B003-10
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BG BR CA CN CZ GE HU IL JP KR LV MX NO NZ PL RO SG SI SK TR UA US
AU 9672120 A 970417 (9732) C11B003-10
ADT DE 19536165 A1 DE 95-19536165 950928; WO 9712017 A1 WO 96-EP4116 960920; AU 9672120 A AU 96-72120 960920
FDT AU 9672120 A Based on WO 9712017
PRAI DE 95-19536165 950928
IC ICM C07C067-56; C11B003-10
ICS A61K047-44; C11C003-00

L11 ANSWER 3 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-178792 [16] WPIDS
DNC C97-057458
TI **Taxol** deriv. prepn. with new intermediates for use in clinical trial(s) in ovarian and metastatic breast cancer - by coupling beta-protected amino carboxylic acid and 13-hydroxy-taxane and deprotecting resulting ester.
DC B02
IN GAO, Y; ZEPP, C M
PA (SEPR-N) SEPRACOR INC
CYC 69
PI WO 9707110 A1 970227 (9716)* EN 44 pp C07D305-14
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA

PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN

AU 9666464 A 970312 (9727) C07D305-14

ADT WO 9707110 A1 WO 96-US12666 960802; AU 9666464 A AU 96-66464 960802
FDT AU 9666464 A Based on WO 9707110
PRAI US 96-589142 960119; US 95-2140 950811
IC ICM C07D305-14
ICS A61K031-335; C07C271-18; C07F007-18

L11 ANSWER 4 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-108882 [10] WPIDS
DNC C97-034750
TI 3-Amino-2-hydroxy-3-phenyl propionic acid deriv. prepn. - in optically active form and high yield by multistage process from phenyl glycine, used as **taxol** intermediate.
DC B05
IN DRAUZ, K; KOTTENHAHN, M; STINGL, K
PA (DEGS) DEGUSSA AG
CYC 25
PI WO 9702236 A1 970123 (9710)* DE 31 pp C07C231-12
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CZ IL JP MX NO US
AU 9663032 A 970205 (9721) C07C231-12
DE 19524337 C1 970507 (9723) C07C233-51
ADT WO 9702236 A1 WO 96-EP2573 960614; AU 9663032 A AU 96-63032 960614; DE 19524337 C1 DE 95-19524337 950704
FDT AU 9663032 A Based on WO 9702236
PRAI DE 95-19524337 950704
IC ICM C07C231-12; C07C233-51
ICS A61K031-195; C07C227-26; C07C229-36; C07C231-14; C07C271-06; C07C275-42; C07D205-10; C07D207-448; C07D209-48; C07D305-14

L11 ANSWER 5 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-077247 [07] WPIDS
DNC C97-024769
TI New 13-acyloxy-7-tri ethyl silyloxy-baccatin III derivs. - useful as intermediates for **paclitaxel**, known anti-leukaemia and tumour inhibiting agent.
DC B02
IN CHANDER, M C; SISTI, N J; SWINDELL, C S
PA (BRYN-N) BRYN MAWR COLLEGE; (NAPR-N) NAPRO BIO THERAPEUTICS INC
CYC 65
PI WO 9640666 A1 961219 (9707)* EN 23 pp C07D305-14
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR CA CN CZ EE FI GE HU IL IS JP KG KP KR LK LR LT LU LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TR TT UA UZ VN
AU 9661706 A 961230 (9716) C07D305-14
ADT WO 9640666 A1 WO 96-US10024 960607; AU 9661706 A AU 96-61706 960607
FDT AU 9661706 A Based on WO 9640666
PRAI US 95-483082 950607
IC ICM C07D305-14

L11 ANSWER 6 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-034076 [03] WPIDS
DNC C97-010591
TI New 2'- and/or 7-substd. **paclitaxel** derivs. - useful for treating cellular proliferative diseases e.g. sarcoma, carcinoma, lymphoma, blastoma, melanomas, myeloma, leukaemia.
DC B02
IN BRESSI, J C; DOUGLASS, J G; SELIGSON, A; SOVAK, M
PA (BIOP-N) BIOPHYSICA FOUND

CYC 70
PI WO 9638138 A1 961205 (9703)* EN 56 pp A61K031-335
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9659622 A 961218 (9714) A61K031-335
ADT WO 9638138 A1 WO 96-US8245 960531; AU 9659622 A AU 96-59622 960531
FDT AU 9659622 A Based on WO 9638138
PRAI US 95-457674 950601
IC ICM A61K031-335
ICS C07D305-14

L11 ANSWER 7 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 97-023092 [03] WPIDS
DNC C97-007480
TI **Taxol** prodrugs are water soluble and inhibit abnormal cell proliferation - e.g. N-de-benzoyl-N-((phosphono-oxymethyl)oxy)carbonyl-2-O-benzoyl-**paclitaxel**, useful in treatment of e.g. cancers and psoriasis.
DC B02
IN KADOW, J F; SCOLA, P M; VYAS, D M
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 23
PI EP 747385 A1 961211 (9703)* EN 26 pp C07F009-655
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CZ 9601563 A3 961211 (9706) C07D305-14
NO 9602231 A 961209 (9707) C07D305-14
AU 9654718 A 961219 (9708) C07F009-38
JP 08337589 A 961224 (9710) 24 pp C07F009-655
CA 2176191 A 961207 (9714) C07F009-655
ADT EP 747385 A1 EP 96-109044 960605; CZ 9601563 A3 CZ 96-1563 960529; NO 9602231 A NO 96-2231 960531; AU 9654718 A AU 96-54718 960605; JP 08337589 A JP 96-139795 960603; CA 2176191 A CA 96-2176191 960509
PRAI US 95-469247 950606
IC ICM C07D305-14; C07F009-38; C07F009-655
ICS A61K031-335; A61K031-66; A61K031-665; C07F009-547; C07F009-6558
ICI C07M007:

L11 ANSWER 8 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 96-443120 [44] WPIDS
DNC C96-139470
TI New 10-deacetyl baccatine III and 10-deacetyl-14 b- hydroxy baccatine III derivs. - have cytotoxic and anti-tumoural activity.
DC B02
IN BOMBARDELLI, E; DE, BELLIS P; GABETTA, B; BELLIS, P
PA (INDE-N) INDENA SPA
CYC 70
PI WO 9629321 A1 960926 (9644)* EN 27 pp C07D305-14
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9648320 A 961008 (9704) C07D305-14
ADT WO 9629321 A1 WO 96-EP904 960304; AU 9648320 A AU 96-48320 960304
FDT AU 9648320 A Based on WO 9629321
PRAI IT 95-MI533 950317
IC ICM C07D305-14
ICS A61K031-335; C07D263-04; C07D493-10; C07F007-18

L11 ANSWER 9 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 96-433740 [43] WPIDS
DNC C96-136140

TI New cephalo-mannine epoxide derivs. have anti-cancer activity - are more active than **taxol** A and may be prepd. by oxidn. of taxane deriv..
DC B02
IN DAUGHENBAUGH, R J; MURRAY, C K; ZHENG, Q Y
PA (HAUS-N) HAUSER CHEM RES INC
CYC 20
PI WO 9628435 A1 960919 (9643)* EN 33 pp C07D305-14
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9653057 A 961002 (9703) C07D305-14
ADT WO 9628435 A1 WO 96-US3242 960308; AU 9653057 A AU 96-53057 960308
FDT AU 9653057 A Based on WO 9628435
PRAI US 95-401711 950310
IC ICM C07D305-14

L11 ANSWER 10 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 96-333281 [33] WPIDS
DNC C96-105286
TI New lipophilic drug derivs. for micellar and liposomal formulations - with drug bonded as ester or amide to di hydroxy- or amino-hydroxy-propyl deriv. of e.g. serine, phospho-choline, glucose.
DC B05
IN ANSELL, S
PA (UYBR-N) UNIV BRITISH COLUMBIA
CYC 1
PI US 5534499 A 960709 (9633)* 11 pp A61K031-70
ADT US 5534499 A US 94-246010 940519
PRAI US 94-246010 940519
IC ICM A61K031-70
ICS A61K009-127; A61K031-715

L11 ANSWER 11 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 96-239429 [24] WPIDS
DNC C96-076423
TI New 3'-des phenyl-**paclitaxel** deriv. taxoid cpds. - used as antitumour agents, effective against drug resistant tumours, e.g. adriamycin-resistant breast cancer..
DC B02
IN OJIMA, I
PA (UYNY) UNIV NEW YORK STATE RES FOUND
CYC 67
PI WO 9613495 A1 960509 (9624)* EN 44 pp C07D305-14
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN
AU 9641330 A 960523 (9635) C07D305-14
EP 788493 A1 970813 (9737) EN C07D305-14
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
ADT WO 9613495 A1 WO 95-US13591 951027; AU 9641330 A AU 96-41330 951027; EP 788493 A1 EP 95-939561 951027, WO 95-US13591 951027
FDT AU 9641330 A Based on WO 9613495; EP 788493 A1 Based on WO 9613495
PRAI US 94-330956 941028
IC ICM C07D305-14
ICS A61K031-335

L11 ANSWER 12 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 96-115642 [12] WPIDS
DNC C96-036575
TI New amino acetoxy methoxy-**paclitaxel** derivs. - used as water-soluble antitumour agents, prepd. e.g. from halo acetoxy methoxy cpd. and amine.

DC B02
IN KADOW, J F; WITTMAN, M D
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 21
PI US 5489589 A 960206 (9612)* 13 pp A61K031-335
EP 716085 A1 960612 (9628) EN 22 pp C07D305-14
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 9540242 A 960613 (9631) C07D305-14
CA 2163706 A 960608 (9639) C07D305-14
JP 08225558 A 960903 (9645) 21 pp C07D305-14
ADT US 5489589 A US 94-350919 941207; EP 716085 A1 EP 95-119300 951207; AU 9540242 A AU 95-40242 951206; CA 2163706 A CA 95-2163706 951124; JP 08225558 A JP 95-318827 951207
PRAI US 94-350919 941207
IC ICM A61K031-335; C07D305-14
ICS A61K031-16; A61K031-165; A61K031-395; A61K031-495; A61K031-535; A61K031-54; C07D405-12; C07D407-12; C07D409-12; C07D413-12; C07D417-12

L11 ANSWER 13 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 95-083403 [12] WPIDS
CR 93-281861 [36]; 93-344999 [43]; 94-110856 [14]; 94-134066 [16]; 94-210176 [26]
DNC C95-037498
TI New taxane derivs. - contain phosphono oxymethyl or methoxy thiomethyl gps. and are antitumour **taxol** analogues.
DC B02 C01 C02
IN GOLIK, J; KADOW, J F; KAPLAN, M A; LI, W; PERRONE, R K; THOTTATHIL, J K; VYAS, D; WITTMAN, M D; WONG, H; WRIGHT, J J; VYAS, D M
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 26
PI EP 639577 A1 950222 (9512)* EN 124 pp C07F009-655
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
NO 9403002 A 950220 (9515) C07F009-38
AU 9470267 A 950302 (9516) C07F009-655
CA 2129288 A 950218 (9520) C07F009-547
FI 9403749 A 950218 (9520) C07F009-655
HU 67742 T 950428 (9523) C07D305-14
JP 07149779 A 950613 (9532) 121 pp C07F009-655
CZ 9401947 A3 950816 (9541) C07D305-14
US 5646176 A 970708 (9733) 58 pp A61K031-38
CN 1111637 A 951115 (9737) C07F009-655
ADT EP 639577 A1 EP 94-112803 940816; NO 9403002 A NO 94-3002 940815; AU 9470267 A AU 94-70267 940815; CA 2129288 A CA 94-2129288 940802; FI 9403749 A FI 94-3749 940815; HU 67742 T HU 94-2342 940812; JP 07149779 A JP 94-250219 940812; CZ 9401947 A3 CZ 94-1947 940811; US 5646176 A CIP of US 92-996445 921224, CIP of US 93-108015 930817, CIP of US 93-154840 931124, Cont of US 94-245119 940517, US 95-445360 950519; CN 1111637 A CN 94-109468 940815
PRAI US 94-245119 940517; US 93-108015 930817; US 93-154840 931124; US 92-996445 921224; US 95-445360 950519
IC ICM A61K031-38; C07D305-14; C07F009-38; C07F009-547; C07F009-655
ICS A61K031-335; A61K031-66; A61K031-665; A61K031-695; C07D405-12; C07D407-12; C07D409-12; C07D413-12; C07D417-12; C07F007-08; C07F007-10; C07F009-117; C07F009-40; C07F009-6558

L11 ANSWER 14 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 94-025897 [03] WPIDS
DNC C94-011933
TI New (meth)acrylamide copolymer bound **paclitaxel** derivs. - used as antitumour agents with high water solubility and low toxicity.
DC A14 A96 B02 B04
IN ANGELUCCI, F; BIASOLI, G; MONGELLI, N; PESENTI, E; SUARATO, A; MONQELLI, N

PA (PHAA) PHARMACIA SPA; (FARM) FARMITALIA ERBA SRL CARLO; (FARM) FARMITALIA ERBA SPA CARLO; (PHAA) PHARMACIA & UPJOHN SPA
CYC 35
PI WO 9400156 A1 940106 (9403)* 32 pp A61K047-48
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BY CA CZ FI HU JP KR KZ NO NZ PL RU UA
FI 9400733 A 940216 (9418) A61K000-00
NO 9400567 A 940218 (9418) A61K047-48
AU 9343233 A 940124 (9420) A61K047-48
EP 600062 A1 940608 (9422) EN A61K047-48
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE
CZ 9400620 A3 940713 (9432) C07D305-14
ZA 9304388 A 941026 (9443) 30 pp A61K000-00
US 5362831 A 941108 (9444) 8 pp A61K031-765
JP 06509822 W 941102 (9503) 12 pp A61K047-48
CN 1079971 A 931229 (9516) C08F222-36
HU 67914 T 950529 (9528) C07D305-14
AU 659750 B 950525 (9529) C08F220-56
AU 9516282 A 950622 (9536) C07K005-062
HU 68959 T 950828 (9540) A61K038-05
US 5473055 A 951205 (9603) 7 pp A61K038-05
TW 266201 A 951221 (9610) C07C231-04
NZ 253116 A 960528 (9626) C07D305-14
AU 671247 B 960815 (9641) C07K005-062
US 5569720 A 961029 (9649) 7 pp C08F020-56
ADT WO 9400156 A1 WO 93-EP1433 930607; FI 9400733 A WO 93-EP1433 930607, FI 94-733 940216; NO 9400567 A WO 93-EP1433 930607, NO 94-567 940218; AU 9343233 A AU 93-43233 930607; EP 600062 A1 EP 93-912905 930607, WO 93-EP1433 930607; CZ 9400620 A3 CZ 94-620 930607; ZA 9304388 A ZA 93-4388 930618; US 5362831 A US 93-77065 930616; JP 06509822 W WO 93-EP1433 930607, JP 94-501981 930607; CN 1079971 A CN 93-107196 930617; HU 67914 T WO 93-EP1433 930607, HU 94-800 930607; AU 659750 B AU 93-43233 930607; AU 9516282 A Div ex AU 93-43233 930607, AU 95-16282 950405; HU 68959 T WO 93-EP1433 930607, Div ex HU 94-800 930607, HU 94-3439 930607; US 5473055 A Div ex US 93-77065 930616, US 94-263832 940622; TW 266201 A TW 93-104130 930525; NZ 253116 A NZ 93-253116 930607, WO 93-EP1433 930607; AU 671247 B Div ex AU 93-43233 930607, AU 95-16282 950405; US 5569720 A Div ex US 93-77065 930616, Div ex US 94-263832 940622, US 95-508210 950727
FDT AU 9343233 A Based on WO 9400156; EP 600062 A1 Based on WO 9400156; JP 06509822 W Based on WO 9400156; HU 67914 T Based on WO 9400156; AU 659750 B Previous Publ. AU 9343233, Based on WO 9400156; HU 68959 T Based on WO 9400156; US 5473055 A Div ex US 5362831; NZ 253116 A Based on WO 9400156; AU 671247 B Previous Publ. AU 9516282; US 5569720 A Div ex US 5362831, Div ex US 5473055
PRAI GB 92-13077 920619
IC ICM A61K000-00; A61K031-765; A61K038-05; A61K047-48; C07C231-04; C07D305-14; C07K005-062; C08F020-56; C08F220-56; C08F222-36
ICS A61K031-16; A61K031-335; A61K031-785; A61K037-02; A61K038-06; A61K038-07; A61K038-08; C07C233-27; C07K005-023; C07K005-04; C07K005-065; C08F008-30; C08F008-32; C08F020-58; C08F222-38; C08G073-06

L11 ANSWER 15 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AN 93-369147 [47] WPIDS
CR 94-083603 [11]; 94-126870 [16]; 96-230983 [24]
DNC C93-163848
TI New mode of admin. of **taxol** to patients suffering from cancer - in lower doses and with shorter admin. times, e.g. over duration of up to 6 hours.
DC B02
IN CANETTO, R M; EISENHAUER, E; ROZENCSWEIG, M; CANETTA, R M; ROZENCWEIG, M; CANETTA, R; CARRETTA, R M
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 22

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PI   AU 641894   B  930930 (9347)*       37 pp    A61K047-28
     ZA 9300686  A  931124 (9401)        44 pp    A61K000-00
     GB 2269319  A  940209 (9404)        41 pp    A61K031-335
     EP 584001   A1 940223 (9408)  EN    17 pp    A61K031-335
        R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     FR 2694192  A1 940204 (9409)        31 pp    A61K031-335
     DE 4325927  A1 940310 (9411)                 A61K031-335
     NL 9301086  A  940301 (9412)        29 pp    A61K031-355
     SE 9301951  A  940207 (9414)                 A61K047-28
     CA 2086874  A  940204 (9416)                 A61K031-335
     PT 101289   A  940429 (9420)                 A61K031-335
     DK 9300652  A  940204 (9421)                 A61K031-335
     BE 1006497  A5 940913 (9439)                 A61K000-00
     JP 07233064 A  950905 (9544)        12 pp    A61K031-335
     CH 686868   A5 960731 (9635)                 A61K031-335
     GB 2269319  B  970409 (9718)                 A61K031-335
     US 5621001  A  970415 (9721)        10 pp    A61K031-335
     EP 584001   B1 970514 (9724)  EN    17 pp    A61K031-335
        R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     DE 69310634 E  970619 (9730)                 A61K031-335
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     EP 783885   A2 970716 (9733)  EN    14 pp    A61K031-335
        R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
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        R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     ES 2101261  T3 970701 (9736)                 A61K031-335
ADT  AU 641894 B AU 93-32102 930129; ZA 9300686 A ZA 93-686 930201; GB
     2269319 A GB 93-15054 930720; EP 584001 A1 EP 93-401978 930729; FR
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     2086874 A CA 93-2086874 930107; PT 101289 A PT 93-101289 930615; DK
     9300652 A DK 93-652 930604; BE 1006497 A5 BE 93-800 930730; JP
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     2269319 B GB 93-15054 930720; US 5621001 A Cont of US 92-923628
     920803, Cont of US 94-232404 940425, US 95-559890 951120; EP 584001
     B1 EP 93-401978 930729; DE 69310634 E DE 93-610634 930729, EP
     93-401978 930729; US 5641803 A Div ex US 92-923628 920803, Cont of
     US 93-109331 930624, US 95-544594 951018; EP 783885 A2 Div ex EP
     93-401978 930729, EP 97-104511 930729; EP 783886 A2 Div ex EP
     93-401978 930729, EP 97-104512 930729; ES 2101261 T3 EP 93-401978
     930729
FDT  DE 69310634 E Based on EP 584001; ES 2101261 T3 Based on EP 584001
PRAI US 92-923628   920803; GB 93-11740    930607; US 94-232404   940425;
     US 95-559890   951120; US 93-109331   930624; US 95-544594   951018
IC   ICM  A61K000-00; A61K031-335; A61K031-355; A61K047-28
     ICS  A61K031-57; A61K035-78; A61K045-00; A61K047-18; A61K047-22
ICI  A61K031-335, A61K031:57; A61K031-335, A61K045:

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L11  ANSWER 1 OF 15  WPIDS   COPYRIGHT 1997 DERWENT INFORMATION LTD
AB   WO 9727855 A   UPAB: 970915
     Enhancing oral absorption of a pharmacologically active taxane to a
     human, comprises co-administering the taxane with cinchonine.
          Also claimed is a composition as above, which comprises a
     taxane, cinchonine and excipients.
          The cinchonine is co-administered orally and simultaneously
     with the taxane. The taxane is selected from paclitaxel
     and docetaxel, where paclitaxel is given at 50 mg/kg and
     cinchonine at 250 mg/kg.
          USE - Taxane can be used for the treatment of tumours,
     particularly in retractory advanced ovarian and breast cancers. They
     can also be used for the treatment of conditions associated with
     abnormal cell proliferation such as psoriasis, solid tumours,
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ovarian, breast, brain, prostate, colon, stomach, kidney and/or testicular cancer, kaposi's sarcoma, choloangiocarcinoma, choriocarcinoma, neuroblastoma, Wilm's tumour, Hodgkin's disease, melanomas, multiple myelomas, chronic lymphatic leukaemia and acute or chronic granulocytic lymphomas. The taxane can be used to prevent or delay the appearance or reappearance of, or to treat these conditions and can also be used for the treatment and prevention of polycystic kidney diseases and rheumatoid arthritis.
Dwg.0/2

L11 ANSWER 2 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB DE19536165 A UPAB: 970512
Purificn. of alkoxylated fats comprises treatment with a solid comprising a mixt. of aluminium oxide and a silicate. Also claimed is the purified prod. obtd.

USE - The prod. is used to produce pharmaceuticals (claimed), as solvents for water insol. active agents, such as pharmaceuticals,esp. **paclitaxel** (**taxol**).
Dwg.0/0

L11 ANSWER 3 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB WO 9707110 A UPAB: 970417
Prepn. of **taxol** (**paclitaxel**) (I) and its derivs.
comprises: (a) reacting a beta -alkoxycarbonylaminophenyl propionic acid of formula (II) with a 13-hydroxy taxane (III) to form a beta -alkoxycarbonylaminophenylpropionic ester at the C13 of the taxane (IV); and (b) cleaving the beta -alkoxycarbonyl in (IV) to give a beta -amido- alpha -hydroxybenzene propanoic ester of the taxane. R1 = 1-10C alkyl, 1-10C alkoxy or opt. substd. phenyl; R3 = H, lower alkyl, lower alkoxy, di-loweralkylamino or halo; R4 = benzyl, t-butyl, allyl, trichloroethyl or 9-fluorenylmethyl. Cpds. of formula (II) and (IV') (see 'Preferred Process') are new.

USE - **Taxol** is currently used in clinical trials in ovarian and metastatic breast cancer.

ADVANTAGE - The process provides an alternative to extn. from Pacific yew bark (Taxus brevifolia).
Dwg.0/0

L11 ANSWER 4 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB WO 9702236 A UPAB: 970307
Prepn. of (2R,3S)- or (2S,3R)-3-amino-2-hydroxy-3-phenylpropionic acid derivs. of formula (I) involves (a) reducing (S)- or (R)-phenylglycine of formula (III) with a hydride reagent, (b) converting the obtd. (S)- or (R)-phenyl-glycinol of formula (IV) into the N-protected deriv. of formula (V), (c) oxidising to the N-protected (S)- or (R)-phenyl-glycinal deriv. of formula (VI), (d) converting (VI) into a (1RS,2S)- or (1RS,2R)-2-amino-1-cyano-2-phenylethane deriv. of formula (VII), (e) hydrolysing (VII) to the acids (or their addn. salts) of formulae (VIII) and (IX); and (f1) converting (VIII) into the (2RS,3S)- or (2RS,3R)-3-amino-2-phenylpropionic acid ester of formula (XII) and protecting the free N of (XIII) to give (I); (f2) converting (IX) into (I); or (f3) N-protecting (VIII) to give (IX) then esterifying to give (I). X = H, 1-6C alkyl or benzyl; Y = 1-6C alkyl, benzyl, CHO, COR1 or COOR2; or X + Y = phthaloyl, maleoyl or maloneyl; R1 = 1-6C alkyl, phenyl, benzyl, NH2, 4-nitrophenyl or 4-nitrobenzyl; R2 = 1-6C alkyl, phenyl, benzyl, 4-nitrophenyl or 4-nitrobenzyl; Z = H, 1-5C alkyl, phenyl, benzyl, 4-nitrobenzyl, 4-nitrophenyl or allyl; n = 0 or 1; W = HCl, HBr or H2SO4; Z' = as Z but not H.

USE - The use of (I), specifically methyl N-benzoyl-3-amino-3-hydroxy-3-phenylpropionate (Ia), for the prepn. of taxols is claimed. (I) are intermediates in the total synthesis of the anticancer agent **taxol** (**paclitaxel**).

ADVANTAGE - (I), esp. the key **taxol** intermediate (Ia), are obtd. in higher yields than in prior art methods, by an

environmentally friendly and economical process.
Dwg.0/0

L11 ANSWER 5 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB WO 9640666 A UPAB: 970212
Paclitaxel intermediates of formula (I) are new. TES = triethylsilyl; P1 = hydrogenatable benzyl protecting gp.

The claimed prepn. of (I) comprises reacting a cpd. of formula (II) with the C7 TES-protected baccatin of formula (III). The reaction takes place in presence of a dialkylcarbodiimide selected from dicyclohexyl carbodiimide or pref. diisopropylcarbodiimide and dimethylaminopyridine in toluene at 80 deg.C for 3-5 hrs.

USE - (I) are useful in an efficient and cost-effective semi-synthesis of **paclitaxel** (by deprotection and acylation), which is a known antileukaemia and tumour inhibiting agent.
Dwg.0/0

L11 ANSWER 6 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB WO 9638138 A UPAB: 970115
A 2'- and/or 7-substd. **paclitaxel** deriv., and its 2' or 7epimer, where the substit. is bonded to O at the 2' or 7 position through an ether or ester bond and is: (i) a 3-12C hydrophilic gp. having at least 1 heteroatom and up to 1 heteroatom per 1.25 C atoms; (ii) a hydrophilic polymer of 5kD, the polymer consisting of monomers having ether, ester and non-oxo-carbonyl side chains; or (iii) an organic molecule of < 2.5kD other than a poly(amino acid) binding specifically to a mammalian cellular receptor of cells susceptible to neoplasia; is new.

USE - The taxoids are useful for reducing the number of neoplastic cells in a combination of cells (claimed). They are useful for treating cellular proliferative diseases, e.g. neoplasias such as sarcomas, carcinomas, lymphomas, blastomas, melanomas, myelomas, Wilms' tumour, leukaemias and adeno-carcinomas. They can be administered in compsns. in conjunction with other chemotherapeutic agents, e.g. antiandrogens, Ca channel blockers, immuno-stimulators, radiation stimulators.

ADVANTAGE - The taxoids are more water-soluble than **paclitaxel** (PT), and have superior pharmacological properties (in an in-vivo study in mice, 7-(2'',3'' dihydroxypropyl oxycarbonyl)**paclitaxel** was 10 times more effective than '**Taxol**' (RTM: PT) against PC-3 tumours, and 2-3 times safer).
Dwg.0/18

L11 ANSWER 7 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB EP 747385 A UPAB: 970320
Paclitaxel prodrugs of formula (I) and their salts are new: R1 = OH, OCORx or OCOORx; R2 = H, OH, OCORx or OCOORx; R2' = H, OH or F; R6' = H or OH; R6 = H; or R2+R6 = oxirane ring or a bond; R3 = H, OH, 1-6C alkoxy, OCONR11R12, OCORx or OCOORx; R8 = Me or CH2OH; or R2+R8 = cyclopropane; R9 = OH or OCORx; one of R7 and R7' = H and the other is OH, OCORx or OCOORx or R7+R7' = oxo; R11, R12 = 1-6C alkyl, H or opt. substd. aryl; R4, R5 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or ZR10; Z = a bond, 1-6C alkyl or 2-6C alkenyl; R10 = opt. substd. aryl, 3-6C cycloalkyl or heteroaryl; Rd, Re = H, 1-6C alkyl, opt. substd. aryl or phosphono protecting gp.; Rf = H or OH; Rx = 3-6C cycloalkyl, 2-6C alkenyl or 1-6C alkyl (all opt. substd. by 1-6 halo) or -D-(C6H3RaRbRc); D = a bond or 1-6C alkyl; Ra-Rc = H, NO2, NH2, 1-6C alkylamino, di(1-6C alkyl)amino, halo, 1-6C alkyl, OH or 1-6C alkoxy; p = 0 or 1; with provisos.

USE - (I) inhibit abnormal cell proliferation of malignant and non-malignant cells in e.g. skin, muscle, bone, brain, sexual organs, the lymphatic system and blood cells. They are useful in the treatment of psoriasis, cancers of e.g. the breast, prostate or colon, Hodgkin's disease, chronic lymphocytic leukaemia and multiple

myeloma.

ADVANTAGE - **Paclitaxel** has very limited water solubility which requires it to be formulated in a non-aqueous carrier. (I) are water soluble which simplifies formulation.

Dwg.0/0

L11 ANSWER 8 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AB WO 9629321 A UPAB: 961104

10-Deacetyl-baccatine III and 10-deacetyl 14beta-hydroxy baccatine III derivs. of formula (I) are new. R1, R2 = H; or R2 = H; and R2 = OH or acetyloxy; or OR1R2 = a cyclic carbonate gp. of formula (i); R3 = alpha or beta-oriented, H or alkylsilyl, pref. triethylsilyl (TES); R4 = H, a residue of formula (ii), or an iso-serine residue of formula (iii); R1' = 1-5C alkyl or alkenyl, or an aryl residue; R2' = 1-5C alkyl or alkenyl, an aryl residue, or a tert-butoxy gp. Syntons of formula (B) and intermediates of formula (9b) are also new.

USE - (I) have cytotoxic and anti-tumoural activity, and may be used in medicaments for treatment of tumours in cardiopathic patients.

ADVANTAGE - (I) show surprising advantages compared with **paclitaxel** on cell lines resistant to other anti-tumoural substances, such as adriamycin or cis-platinum. (I) are devoid of cardiotoxic activity, contrary to **taxol** and its derivs.

Dwg.0/0

L11 ANSWER 9 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AB WO 9628435 A UPAB: 961025

Cephalomannine epoxide or 10-deacetyl **taxol** B epoxide derivs. of formula (I) are new. R = H or acetyl; R1-R3 = H or alkyl.

USE - (I) have anticancer activity (claimed).

ADVANTAGE - (I) are more active than **paclitaxel** (**taxol** A).

Dwg.0/9

L11 ANSWER 10 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AB US 5534499 A UPAB: 960823

Lipophilic drug derivatives of the formula (I) and (II) are new. A = a serine, ethanolamine, choline, phosphocholine, phosphoserine, phosphoethanolamine, glycerol, phosphoglycerol, inositol or phosphoinositol radical, NR1R2, OCOR3, OH, O-glucose, O-galactose or O-oligosaccharide; R1, R2 = H or 1-6C alkyl; R3 = opt. unsaturated alkyl; X, X' = opt. unsatd. alkyl or opt. unsatd. alkylene; Y, Y' = -S-, -NH-, -NHCO-, -CO(CH2)pCO2-, -O-, =NNHCO-, -CO- or -CO(CH2)pCONH-; p = 0-8; Z, Z' = a therapeutic agent; m, n = 0 or 1; m+n is at least one.

Also claimed are pharmaceutical compsns. comprising (I) or (II) in a micellar or liposomal formulation.

USE - (I) and (II) are esp. derivs. of **paclitaxel**, doxorubicin or podophyllotoxin (claimed). (I) and (II) are useful derivs. of cpds. which are difficult to formulate, esp. **taxol** derivs. The linkage between the therapeutic agent and the lipid can be cleaved in vivo, allowing the agent to be separated from the micellar or liposomal formulation.

A soln. of the liposomes suspended in an aq. carrier may be administered intravenously.

Dwg.0/0

L11 ANSWER 11 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AB WO 9613495 A UPAB: 960618

C-3' -Alk(en)yl taxoid cpds. of formula (I) are new. R1=3-5C alkyl or alkenyl gp.; R2=3-5C branched alkyl; R3,R4=H or protecting gp. including functional gps. which increase the water-solubility of (I); R5=H, acyl, alkoxycarbonyl or carbamoyl; R6=acyl.

USE - (I) are antineoplastic/antitumour agents, esp. used for

treating leukaemia, melanoma, non-small cell lung, breast, ovarian and colon cancers (all claimed). They are also precursors for other antitumour agents. (I) are administered orally, parenterally or topically. No dosage ranges are given.

ADVANTAGE - (I) have stronger activity than **paclitaxel** or docetaxel against drug-resistant tumours, e.g. more than an order of magnitude higher activity against adriamycin-resistant breast cancer. They also have fewer undesirable side-effects, better pharmacological properties and/or improved activity spectra.
Dwg.0/0

L11 ANSWER 12 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB US 5489589 A UPAB: 960322
Aminoacetoxy(poly)methoxy-substd. **paclitaxel** derivs. of formula (I) and their salts are new. R1, R2 = H or -(CH2O)nCOCH2Y (a); R6 = H, 1-8C alkanoyl or (a); n = 1-6; p = 0 or 1; R4, R5 = 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl or -Z-R7; Z = direct bond, 1-8C alkylene or 2-8C alkenediyl; R7 = aryl (opt. substd.), 3-8C cycloalkyl or heteroaryl; R3 = H, 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, 3-8C cycloalkyl, aryl or heteroaryl; Y = NR'R', aziridino, azetidino, pyrrolidino, 4-(R')-piperazino, morpholino or thiamorpholino; R' = H or 1-8C alkyl; provided that at least one of R1, R2 and R6 = (a).

Pref. one of R1, R2 = (a) and the other = H; R3 = Me; R4, R5 = Ph; R6 = acetyl; p = 0.

USE - (I) are antitumour agents (claimed). They are used for the same treatments as **paclitaxel**.

Dose is 1-100 mg/kg, pref. parenterally.

ADVANTAGE - (I) are water-soluble (unlike the parent cpd. **paclitaxel**).
Dwg.0/0

L11 ANSWER 13 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB EP 639577 A UPAB: 950328
Taxane derivs. contg. phosphonooxymethyl (POM) or methylthiomethyl (MTM) ether gps. and of formulae (A) (T-(OCH2(OCH2)OP(=O)(OH)2)n; (B) T'-(OCH2(OCH2)mSMe)n; (C) T'-(OCH2(OCH2)mOP(=O)(ORy)2)n; and (D) (13-OM)-Txn-(OCH2(OCH2)mSMe)n and their salts, are new. In the formulae, T = a taxane moiety substd. at C-13 by a substd. 3-amino-2-hydroxypropanoyloxy gp.; T' = T in which non-reacting hydroxy gps. have been blocked; Txn = a taxane nucleus; M = H or a metal; m = 0-6; and n = 1-3.

Also new are certain cpds. related to (B), but in which the hydroxyls are not, or not all, blocked.

USE - (A) are analogues of **taxol** (also called **paclitaxel**), and are antitumour agents. It is believed that they are actually prodrugs, with the solubilising POM1 gp. split off in vivo by phosphatase. The remaining (B), and (C) and (D), are intermediates for (A) and active (B), of which both find use in both human and veterinary medicine as tumour inhibitors. Dosage is pref. parenteral, 1-100 mg/kg; or 5-500 mg/kg orally.

ADVANTAGE - The POM gp. provides aq. solubility, making formulation partic. for injections, easier.
Dwg.0/0

L11 ANSWER 14 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD
AB WO 9400156 A UPAB: 970220
Novel polymer conjugates (I) comprise: (A) 90-99.9 mol.% N-(2-hydroxypropyl)-methacrylamide units of formula Me-C(CH2)-CONHCH2CH(OH)2Me (I); (B) 0.1-5 mol.% paclitoxel (i.e. **taxol**) residue-contg. N-substd. methacrylamide units of formula Me-C(CH2)-CONHCH2COA1NHCH2CH(OH)Me (II); and opt. (C) 0-9.9 mol.% N-substd. methacrylamide units of formula (III): one of R1, R2 is copolymer residue of formula -CH2-CMe(CONHCH2COA)- and the other is H; R is Ph or t-BuO; R3 is H or acetyl; A, A1 = direct bond or

aminoacid or peptide spacer selected from Beta-Ala, Gly, Phe-Gly, Phe-Phe, Leu-Gly, Val-Ala, Phe-Ala, Leu-Phe, Leu-Ala, Phe-Leu-Gly, Phe-Phe-Leu, Leu-Leu-Gly, Phe-Tyr-Ala, Phe-Gly-Phe, Phe-Phe-Gly, Phe-Leu-Gly-Phe, Gly-Phe-Leu-Gly-Phe, Gly-betaAla, Phe-Gly-betaAla, Phe-Phe-betaAla, Leu-Gly-betaAla, Val-Ala-betaAla, Phe-Ala-betaAla, Leu-Phe-betaAla, Leu-Gly-betaAla, Phe-Leu-Gly-betaAla, Phe-Phe-Leu-betaAla, Leu-Leu-Gly, betaAla, Phe-Tyr-Ala-betaAla, Phe-Gly-Phe-betaAla, Phe-Phe-Gly-betaAla, Phe-Leu-Gly-Phe-betaAla or Gly- Phe-Leu-Gly-Phe-betaAla.

Also new are **paclitaxel** derivs. (II') having formula (II) in which (i) R1 = -A'2-H (where A'2 = di-, tri- or tetrapeptide spacer as defined for A) and R2 = H or (ii) R1 = H and R2 = -A'3-H (where A'3 = betaAla or di-, tri- or tetrapeptide spacer as defined for A).

USE/ADVANTAGE - (I) are derivs. of the antitumour agent **paclitaxel** (**taxol**) which have higher water-solubility and lower toxicity than the parent cpd.,and are thus suitable for intravenous injection or infusion. (I) are cleared within the cell to release active agent, and show antitumour activity against e.g, Sarcoma, carcinoma, lymphoma, neuroblastoma, myeloma, Wilms tumour, leukaemia and adenocarcinoma. Dosage is 1-1000 (pref. 4-800) mg/kg i.v. (II') are intermediates for (I). They are also useful as antitumour agents having higher water-solublity and lower toxicity than **paclitaxel**.

Dwg.0/0

L11 ANSWER 15 OF 15 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AB AU 641894 B UPAB: 960625

Admin. of **taxol** to a patient suffering from cancer comprises infusing **taxol** (135-175 mg/m2) over a duration not exceeding 6 hrs..

USE/ADVANTAGE - The method requires less **taxol** and less admin. time than prior art methods. It is esp. suitable for treatment of overian cancer. It causes less myelosupression and lower incidence of fever and infection than prior art methods. It is also possible to administer **taxol** on an outpatient basis (earlier processes required) hospitalisation which cuts down on expense and improves patient quality of life. Admin. esp. comprises infusion of 135 mg/m2 of **taxol** over a period of up to 3 hrs.

Dwg.0/0

Dwg.0/0